to grow just a spinal segment or two could translate into dramatic quality-of-life improvements. For instance, short-distance restoration of spinal circuitry could allow patients with cervical injuries to breathe independently without a respirator, or those who have sustained lumbar injuries to increase mobility and regain bowel and bladder function. The field of CNS regeneration is alive and bursting with potential; the next decade holds the promise of exciting progress.

References

1. Ferretti, P., Zhang, F., and O'Neill, P. (2003). Changes in spinal cord regenerative ability through phylogenesis and development: lessons to be learnt. Dev. Dyn. *226*, 245–256.
2. Goldberg, J.L., Klassen, M.P., Hua, Y., and Barres, B.A. (2002). Amacrine-signaled loss of intrinsic axon growth ability by retinal ganglion cells. Science *296*, 1860–1864.
3. Neumann, S., and Woolf, C.J. (1999). Regeneration of dorsal column fibers into and beyond the lesion site following adult spinal cord injury. Neuron *23*, 83–91.
4. Spencer, T., and Filbin, M.T. (2004). A role for cAMP in regeneration of the adult mammalian CNS. J. Anat. *204*, 49–55.
5. Ramer, L.M., Ramer, M.S., and Steeves, J.D. (2005). Setting the stage for functional repair of spinal cord injuries: a cast of thousands. Spinal Cord *43*, 134–161.
6. David, S., and Aguayo, A.J. (1981). Axonal elongation into peripheral nervous system “bridges” after central nervous system injury in adult rats. Science *214*, 931–933.
7. Ramer, M.S., Priestley, J.V., and McMahon, S.B. (2000). Functional regeneration of sensory axons into the adult spinal cord. Nature *403*, 312–316.
8. Silver, J., and Miller, J.H. (2004). Regeneration beyond the glial scar. Nat. Rev. Neurosci. *5*, 146–156.
9. Bradbury, E.J., Moon, L.D., Popat, R.J., King, V.R., Bennett, G.S., Patel, P.N., Fawcett, J.W., and McMahon, S.B. (2002). Chondroitinase ABC promotes functional recovery after spinal cord injury. Nature *416*, 636–640.
10. Caroni, P., and Schwab, M.E. (1988). Two membrane protein fractions from rat central myelin with inhibitory properties for neurite growth and fibroblast spreading. J. Cell Biol. *106*, 1281–1288.
11. He, Z., and Koprivica, V. (2004). The Nogo signaling pathway for regeneration block. Annu. Rev. Neurosci. *27*, 341–368.
12. Filbin, M.T. (2003). Myelin-associated inhibitors of axonal regeneration in the adult mammalian CNS. Nat. Rev. Neurosci. *4*, 703–713.
13. Mandemakers, W.J., and Barres, B.A. (2005). Axon regeneration: it's getting crowded at the gates of TROY. Curr. Biol. *15*, R302–R305.
14. Lee, D.H., Strittmatter, S.M., and Sah, D.W. (2003). Targeting the Nogo receptor to treat central nervous system injuries. Nat. Rev. Drug Discov. *2*, 872–878.
15. Woolf, C.J. (2003). No Nogo: now where to go? Neuron *38*, 153–156.
16. Zheng, B., Atwal, J., Ho, C., Case, L., He, X.L., Garcia, K.C., Steward, O., and Tessier-Lavigne, M. (2005). Genetic deletion of the Nogo receptor does not reduce neurite inhibition in vitro or promote corticospinal tract regeneration in vivo. Proc. Natl. Acad. Sci. USA *102*, 1205–1210.
17. Tessier-Lavigne, M., and Goodman, C.S. (1996). The molecular biology of axon guidance. Science *274*, 1123–1133.
18. De Winter, F., Oudega, M., Lankhorst, A.J., Hamers, F.P., Blits, B., Ruitenberg, M.J., Pasterkamp, R.J., Gispen, W.H., and Verhaagen, J. (2002). Injury-induced class 3 semaphorin expression in the rat spinal cord. Exp. Neurol. *175*, 61–75.
19. Koeberle, P.D., and Bahr, M. (2004). Growth and guidance cues for regenerating axons: where have they gone? J. Neurobiol. *59*, 162–180.
20. Goldshmit, Y., Galea, M.P., Wise, G., Bartlett, P.F., and Turnley, A.M. (2004). Axonal regeneration and lack of astrocytic gliosis in EphA4-deficient mice. J. Neurosci. *24*, 10064–10073.
21. Goldberg, J.L., Vargas, M.E., Wang, J.T., Mandemakers, W., Oster, S.F., Sretavan, D.W., and Barres, B.A. (2004). An oligodendrocyte lineage-specific semaphorin, Sema5A, inhibits axon growth by retinal ganglion cells. J. Neurosci. *24*, 4989–4999.
22. Moreau-Fauvarque, C., Kumanogoh, A., Camand, E., Jaillard, C., Barbin, G., Boquet, I., Love, C., Jones, E.Y., Kikutani, H., Lubetzki, C., *et al*. (2003). The transmembrane semaphorin Sema4D/CD100, an inhibitor of axonal growth, is expressed on oligodendrocytes and upregulated after CNS lesion. J. Neurosci. *23*, 9229–9239.
23. Benson, M.D., Romero, M.I., Lush, M.E., Lu, Q.R., Henkemeyer, M., and Parada, L.F. (2005). Ephrin-B3 is a myelin-based inhibitor of neurite outgrowth. Proc. Natl. Acad. Sci. USA *102*, 10694–10699.
24. Breasted, J.H. (1980). The Edwin Smith surgical papyrus (Chicago: University of Chicago Press).

Division of Research, Genentech Inc., 1 DNA Way, South San Francisco, California 94080, USA.
E-mail: laure@stanford.edu

Correspondences

Requirement for high-level processing in subliminal learning

Aaron Seitz[1], Christine Lefebvre[2], Takeo Watanabe[1] and Pierre Jolicoeur[2]

We are constantly learning new things as we go about our lives, and refining our sensory abilities. How and when these sensory modifications take place is the focus of intense study and we report here that even subliminal learning, which occurs without awareness of what is learned, requires high-level processing.

Some researchers have proposed that sensory plasticity can only take place on features a person attends to [1,2], but others have shown sensory improvements can occur for unattended features [3,4]. In the latter case, subliminal motion vectors were learned when they were temporally correlated with the targets of the subject's task [3]. This led to the view that successful recognition of the task-targets triggers a diffuse learning signal that enables learning of features temporally correlated with the task-targets. We have directly tested this proposition to ascertain what level of processing is required for this subliminal learning.

We used the attentional blink paradigm [5]: an imbalance in identification accuracy of two masked targets presented in rapid succession; the first target is seen but the second not. The attentional blink is mostly studied within the context of a rapid serial visual presentation (RSVP). For example, in our experiment, participants were trained on the identification of two target digits (T_1, T_2) presented within a series of distractor letters (Figure 1). Each stimulus is presented for 100 ms, and subjects must hold

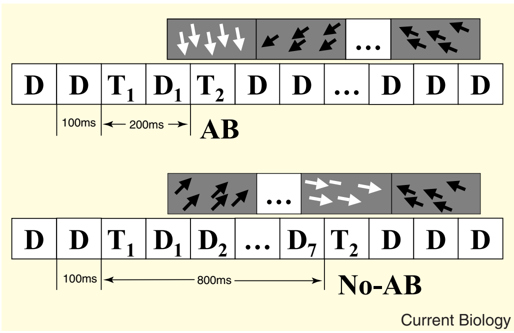

Figure 1. Attentional blink training task.

In the RSVP task, a series of 15–20 characters were presented in rapid succession with a stimulus onset asynchrony (SOA) of 100 ms between letters. In the **AB** condition (top), a single intervening distractor (D) was presented between T_1 and T_2, producing a T_1–T_2 SOA of 200 ms. In the **NoAB** condition (bottom), seven intervening distractors ($D_{1\text{-}7}$) were presented between T_1 and T_2, producing a T_1–T_2 SOA of 800 ms. On each trial, a random sequence of five dot patterns (arrows) with 5% coherent motion commenced with a SOA of 150 ms from T_1 onset, with each direction presented for 200 ms thereafter. For each subject, two different directions (white arrows) were randomly assigned to be paired with T_2.

their response until the end of the 15–20 character sequence. When a short stimulus onset asynchrony (SOA) of 200 ms separates the two targets, the second target (T_2) is less likely to be reported correctly than when 800 ms separates the two targets. This difference is called the attentional blink effect (Figure 2); it is very robust and has been shown in hundreds of experiments [6].

The attentional blink is believed to reflect the processing capacity limitation of our high-level processing-stages [7–8]. While

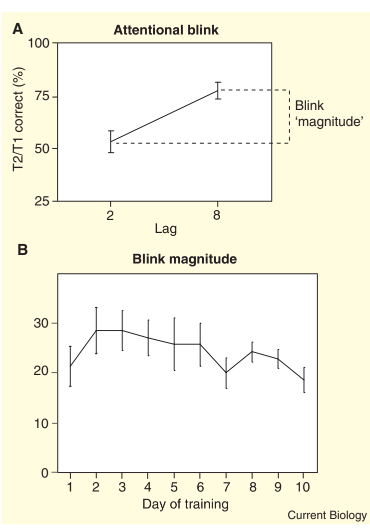

Figure 2. The attentional blink.

(A) Performance on T_2 when T_1 is correct, on lag 2 and lag 8, averaged over all participants and all sessions. The difference in performance between lag 8 and lag 2 is labeled blink magnitude. (B) Average magnitude of blink on each day of training (accuracy at 800 ms SOA minus accuracy at 200 ms SOA). The error bars represent standard error.

certain high-level systems suffer from this 'processing-bottleneck' and cannot perform multiple functions concurrently, other lower-level processing stages do not have the same limitations [9,10]. For instance, perceptual and semantical processing for the 'blinked' target has been verified through behavioral [10] and electrophysiological [9] measures. The fact that the semantic identity of the 'blinked' target is determined, but still goes unreported, suggests the attentional blink is caused by a failure of memory. Other lines of evidence indicate that the processing bottleneck is central to multiple high-level processes, including short-term memory consolidation, response selection and other decision processes [8,11].

Whether subliminal learning takes place during the attentional blink is an important clue to the level of processing required for learning. If learning occurs during the blink, it would indicate that perceptual processing and target recognition are sufficient for learning; but if no learning occurs during the blink, it would indicate that a high level of processing, at or beyond the level of the bottleneck, is required.

To test this we designed a subliminal learning experiment in which each subject was 'subliminally trained' on two different directions of motion: one presented within the window of the attentional blink and the other outside the blink window. We presented irrelevant, unattended moving dots, with 5% motion direction coherence, peripherally while subjects conducted the RSVP task. In trials when a short SOA separated the two targets (**AB** condition), a particular direction of motion was temporally paired with T_2. When the SOA was long (**NoAB** condition) a different direction of motion was temporally paired with T_2. A control set of directions was presented with distractor letters and the motion stream commenced after occurrence of T_1 so that no direction was paired with T_1. Participants were tested on a motion identification task before and after 10 days of training with the dual target RSVP task.

The results support the view that a high level of processing of T_2 is required for subliminal learning on the direction paired with T_2. In the **NoAB** condition a clear effect of learning was observed for the direction paired with T_2 (Figure 3A). This can be seen by comparing the psychometric contrast response curves on the first and last day of testing. A three-way ANOVA shows a significant interaction between day of testing and direction ($F(1,6) = 8$, $MSE = 0.01$ $p < 0.05$). Decomposition of this interaction shows performances are significantly higher after (63% correct) than before (51% correct) training in the **NoAB** condition, ($F(1,6) = 45.48$, $MSE = 0.00$, $p < 0.001$) These results accord with previous studies of task-irrelevant learning [3,4] and show that the subjects are capable of learning under these conditions. But no learning (55% vs 51%; $p = 0.32$) was found for the direction paired in the **AB** condition (Figure 2B).

These results suggest there is a high-level gating mechanism for learning that is affected by the attentional blink. A difficulty for this view is that attentional processing of the first target resulted in impeded stimulus processing of the **AB** direction. In this scenario, a learning signal could be released during the **AB**, but learning would fail due to the impoverished processing of the

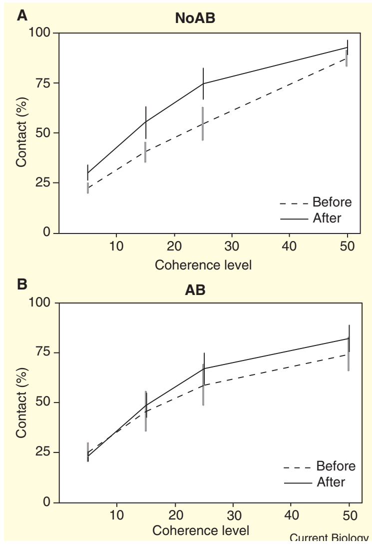

Figure 3. Performance of seven subjects on direction discrimination task before (dotted lines) and after (continuous lines) subliminal training.

(A) For the motion direction paired with T_2 of the **NoAB** condition, improved performance after training is observed across all levels of tested motion coherence. (B) For the motion direction paired with T_2 of the **AB** condition, no clear performance change was observed. The bars represent standard errors.

AB direction compared to the **NoAB** direction. To control for this possibility we introduced a control task, using a new set of subjects, to test if there was a reduced ability of subjects to report the **AB** direction. Subjects were required to give an immediate report of the motion direction paired with T_2. The stimulus sequence and task constraints, until motion offset, of this control were identical to the main task, so any differences in stimulus processing between the **AB** and **NoAB** directions should be revealed as performance differences in motion direction identification. Task performance at 5% coherence (used for training) was poor both for the **AB** and **NoAB** conditions but surprisingly was slightly, but significantly, better for the **AB** direction (**NoAB** = 15.6 ± 4.4 vs **AB =** 22.9 ± 5.8; $p < 0.01$ t test). While this result is opposite to that predicted by the low-level hypothesis, it was not unexpected as the **NoAB** direction is later in the motion stream and is likely subject to forward masking. This rules out all possible confounds of a low-level stimulus processing deficit during the blink.

Although it had been hypothesized that successful recognition of a task-target leads to the release of a diffuse learning signal, resulting in learning for those features temporally correlated with that target [3], until now we lacked a framework by which to identify the requirements for this signal to be released. We have shown the bottleneck believed to be responsible for the attentional blink encompasses processes critical for perceptual learning. We suggest that a high level processing stage limited by the attentional blink gates the release of a non spatially or featurally specific learning signal. This signal effects learning of low-level stimulus features.

Our results have potentially important implications for other types of learning and attentional processes. They help reconcile results of subliminal learning with attentional learning theories. Subliminal learning may involve attentional processing, but attention does not need to be directed to a feature for that feature to be learned. This is consistent with data indicating that attention involves multiple, but distinct, subsystems [12,13] and findings that an array of different processes are limited by the blink [11]. While some of these attentional systems are featurally specific, others are not and may account for subliminal learning [14]. This unification of these two lines of research is an important step toward increasing our understanding of the mechanisms that underlie our ability to direct attention to important environmental factors and to learn from them.

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Supplemental data
Supplemental data including experimental procedures are available at http://www.current-biology.com/cgi/content/full/15/18/R753/DC1/

References
1. Ahissar, M., and Hochstein, S. (1993). Attentional control of early perceptual learning. Proc. Natl. Acad. Sci. USA *90*, 5718–5722.
2. Shiu, L.P., and Pashler, H. (1992). Improvement in line orientation discrimination is retinally local but dependent on cognitive set. Percept. Psychophys. *52*, 582–588.
3. Seitz, A.R., and Watanabe, T. (2003). Psychophysics: Is subliminal learning really passive? Nature *422*, 36.
4. Watanabe, T., Nanez, J.E., and Sasaki, Y. (2001). Perceptual learning without perception. Nature *413*, 844–848.
5. Weichselgartner, E., and Sperling, G. (1987). Dynamics of automatic and controlled visual attention. Science *238*, 778–780.
6. Shapiro, K. (2001). The limits of attention: temporal constraints in human information processing (Oxford; New York: Oxford University Press).
7. Chun, M.M., and Potter, M.C. (1995). A two-stage model for multiple target detection in rapid serial visual presentation. J. Exp. Psychol. Hum. Percept. Perform. *21*, 109–127.
8. Jolicoeur, P. (1999). Restricted attentional capacity between sensory modalities. Psychon. Bull. Rev. *6*, 87–92.
9. Luck, S.J., Vogel, E.K., and Shapiro, K.L. (1996). Word meanings can be accessed but not reported during the attentional blink. Nature *383*, 616–618.
10. Shapiro, K.L., Driver, J., Ward, R., and Sorensen, R.E. (1997). Priming from the attentional blink: A failure to extract visual tokens but not visual types. Psychol. Sci. *8*, 95–100.
11. Jolicoeur, P. (1998). Modulation of the attentional blink by on-line response selection: evidence from speeded and unspeeded task decisions. Mem. Cognit. *26*, 1014–1032.
12. Fan, J., McCandliss, B.D., Sommer, T., Raz, A., and Posner, M.I. (2002). Testing the efficiency and independence of attentional networks. J. Cogn. Neurosci. *14*, 340–347.
13. Posner, M.I., and Petersen, S.E. (1990). The attention system of the human brain. Annu. Rev. Neurosci. *13*, 25–42.
14. Seitz, A., and Watanabe, T. (2005). A unified model for perceptual learning. Trends Cogn. Sci. *9*, 329–334.

[1]Department of Psychology, Boston University, Boston MA 02215, USA
[2]Département de Psychologie, Université de Montréal, Montreal QC H3C 3J7, Canada.